

EcoR I

ECOR T

~~~~~

|       |              |             |             |             |            |
|-------|--------------|-------------|-------------|-------------|------------|
| -4152 | AGGAATTTCAT  | CCATTTAAAT  | CATACAATTT  | AATGGCTTTT  | AGTATATTCA |
| -4102 | CAGGTTGTGC   | ATCCATCACA  | ATCCATTTTA  | GAACAGTTTT  | ATTACTCCAA |
|       | <HNF-3/Fkh-1 |             | SREBP>      |             |            |
| -4052 | AAATAAAACCC  | TGCATTCCCT  | AGCCATCACC  | CCCCAACATC  | CTCCATCCTC |
|       |              |             | NF-Y>       |             |            |
| -4002 | CTTCCAAGCC   | CTGGGCAACC  | ACCAATCTAC  | TTTCTGTCTC  | TATAAATTTG |
| -3952 | CCAATTCTGG   | ACATTTTCATA | TAAATGGAAG  | CAAACAACAT  | GTGAGACTTT |
|       | <NF-Y        | <IRF-2      |             |             |            |
| -3902 | GTGACTGGCT   | GCTTTTCACTT | AGCATTCTAT  | TTTTAAGGCT  | CATTATGTTA |
| -3852 | CAGTACTTAG   | CAGTACTTCA  | TTC'TTTTTTA | TTCTCAAATG  | GTATTCCACT |
| -3802 | GTGTGGGTAT   | CCCATATCAT  | ATTATTAGAG  | ACAGGTTCTC  | ACTCTGTCAC |
| -3752 | CCAGGCTGGA   | GTGCAGTGGC  | ACAATCATAG  | CTCACTGTAA  | CCTCAAACCT |
|       |              | <SREBP      |             |             |            |
| -3702 | CTGGGCTCAA   | GTGATCCTAC  | TACCTCAGCC  | TCCAGAGTAG  | CTAGGACTAC |
|       |              |             |             |             | <IRF-1     |
| -3652 | AGGCACACAC   | AGCCATACCT  | GGCTAATTTT  | TTTTTTTAAAT | TTTCATTTTA |
| -3602 | TGTATTCATT   | TTCTTTCTTT  | TTTGTTGTTG  | TTGTTTTGAG  | ATAGGGTCTC |
| -3552 | ACTTTGTTAC   | CCAGGCTGGA  | GGGCAGTGGC  | ATGGTGACAG  | CTGAGCAGCC |
|       |              | <SREBP      |             |             |            |
| -3502 | TTGACTTCCT   | GGGCTCAAGT  | GATCCTCCTG  | CCTCAGCCTC  | CCAAGTAGCT |
| -3452 | GGGACTACAA   | ACACGTGTCA  | CCATGCCTGG  | CTGATATTTT  | TTTTCTTGAA |
| -3402 | ACAGGGTATC   | ACTCTGTTGC  | CCAGGCTGGA  | GTACAGTGGC  | GTAATAATAG |
|       | c1           |             |             |             |            |
|       | Pst I        |             |             |             |            |
|       | ~~~~~        |             |             |             |            |
| -3352 | CTCACTGCAG   | CTTCCCCTCC  | TGGGCTCAAG  | CAATCCGCTG  | GCCTCAGCAT |
| -3302 | CCTGAGTAGC   | TGGGACTACA  | GGCTTG TGCC | ACCAGGCCCA  | GCTAAGTTTT |
| -3252 | AAAAAATGAT   | TTTTTGGTATA | GAGGAGGTCT  | TGCTATGTTG  | CTCAGGCTGT |
|       |              |             |             |             | SREBP>     |
| -3202 | ATTTTTATTG   | TTGAGACAAG  | GTCTCACTAT  | GTTGCCATGA  | TCCCCCACC  |
|       |              |             |             | <AP-1       |            |
| -3152 | TCCACTTCCC   | AAAGTGCTCA  | TCTTATCTGT  | TCATTAGTCA  | GTTGACAGAC |
|       |              |             | <RAR-α1     |             |            |
| -3102 | ATTTAGGTTG   | TTTCCACTTT  | TTGACCATTA  | TGAATAATAC  | TCCAGTGAAT |
| -3052 | ATTTCATGTAT  | ACATTTGTGT  | GGGCATATGT  | TTTCATTCT   | GTTGGGTTTA |
| -3002 | TATCTAGGAG   | TGGAATTGCT  | GGATCCCGGG  | TAATATTTTG  | ACAGGCAGAG |
|       |              |             |             | C/EBP-β>    |            |
| -2952 | TTCAGGGGAA   | GAAAAACTTG  | GGAAAATGAA  | GCATGTTTAG  | AAATCAGCAA |
| -2902 | GAGTGCAGGG   | GTTTTTCGGA  | GTTTTATTTT  | ATATTCTGTT  | GACAAATGTG |
| -2852 | CAGTTTGATG   | AAGATACAAG  | TTATACTAAG  | TGAGAAGTCA  | GAATTAAGGC |
| -2802 | TGGAATAGGG   | CGTTCAGAGT  | AAAATCATGA  | AGCACTTTGA  | ATACCAAAT  |
|       |              | NF-1>       | <HNF3-β     |             |            |
| -2752 | TAAGGAGCTT   | GGCTGTAAAC  | AAAATAATAA  | AAAATCACAA  | TTTTTTTTTT |
| -2702 | TTTTTTTGAGA  | AAGAGTCTTG  | CTCTTTCACC  | CTGGCTGGAG  | GGCAGTGGTG |
|       | <SREBP       |             |             |             |            |
| -2652 | TGATCTCAGC   | TCACTGCAAC  | TTTCGCCTCC  | CGGGTTCAAG  | CAATTCCTCT |

2020/06/02

| Position | Sequence                                                               | Transcription Factor |
|----------|------------------------------------------------------------------------|----------------------|
| -2602    | GCTTCAGCCT CCAAGTAGC TGGGACTACA GGCAC <u>TCCC</u> ACCATGCCCA           | <NF-kB><IRF-1        |
| -2552    | GCTGATTTTT GTATTTTTAG TAGAGATGGG <u>ATTTC</u> ACTTT GTTGGCCAAG         |                      |
| -2502    | CTGGTCTCAA ACTTTTTGCT GTCATAATTG TTGTA <u>ACTAT</u> TGTTCTTTTT         | AP-2> <HNF3-β        |
| -2452    | GCTGAGGTAG GG <u>CCCCC</u> CAGA CCA <u>AAAAA</u> TAAATCTTAG AATCCAAATC |                      |
| -2402    | AGTGTGTTGG TTTGACCACT GTCACTTGAG AACCACAGTG TGACCAGGGC                 | C2<br>Taq I<br>~~~~~ |
| -2352    | CTCAGGAGTA GAGGTGATCT CTGCTCGAAA GAG <u>AAAT</u> AGTA ATGAAATAT        | IRF-2>               |
| -2302    | TCTCCGGGCC AGGCGTGGTG GCTCATGCCT GTAATCCAG CACTTTGGGA                  | <Whn<br>T3R>         |
| -2252    | GGCCAAGGCA TGTGGATCAG CTGAGGTCAG GAGTTCAAAA CCAGCCTGGC                 | SREBP> RAR-α1>       |
| -2202    | CAACATGGTG AAACCCCGTC TCTACTAAAA ATACAAAAAA TTAGCTAAGT                 |                      |
| -2152    | GTGGTGGCGC ATGCCTGTAA TCCCAGCTAC TTGGGAGGGT GAGGCAGGAG                 | <Pax-6 SREBP>        |
| -2052    | AATTTCTTGA ACCCGGGAGG CAGAGGTTGC AGTGAAGCGA GATC <u>ACACCA</u>         | <AP-2 <HNF-3/Fkh-2   |
| -2002    | CTGCACTCCA GCCTGGGGGA GAGAGCGAGA CTTCTCTCA AAAAA <u>CAAA</u>           | C/EBP-β> <CHOP       |
| -1952    | AAACAAAAGA ATTAAGCAAA TTAGACATTG CAGAGAGAAC CTGAAGGGGC                 | RAR-α1> <NF-1 Pax-6> |
| -1902    | TCAGACCACG TACAGATTTC TGTGCCACAT GCGCAAGTACT TCTGAGGCAT                |                      |
| -1852    | GACTGGATGA GCTGTCCACA TCTGAAATCA TCCAGTCTTG TTCAGAACTT                 | RAR-α1>              |
| -1802    | TCACACCGGA CAGGGAGCCA GGACTGGAAT GCAGTCTCCT GGTCACTGGC                 | NF-1> <ER <NF-1      |
| -1752    | CAGAGAGTTG GCCTTGACCC TGAGACCAGT GGCCAACAAA GGAGCTGCTT                 | <Rel AP-1>           |
| -1702    | AGTCTACCTC CCAGGAAATC CCAGGTGCTT GTCTTCTCTGG GAAGTGAATC                | <NF-1                |
| -1652    | ATTGGCGCAG CACTCCGTAT TTTCTCCTCT TCCCAGGGGA AGGATCCTAG                 | <GR                  |
| -1602    | GGCAGTATTT GGGAAAGACA TGGGCATGGA AGGACACCGG GTGAATGCAT                 | C3<br>Sac I<br>~~~~~ |
| -1552    | AGCCTGCCTG GTTCTGAGCT CTCATGGTAA GGCTCCTACA GACACGGAAA                 |                      |
| -1502    | AGATGGGGGC ACAGGGACAG ATCAGTAGGG TCAGAGCATC TCAGGGACCG                 |                      |
| -1452    | AGGGCAATAT GGTCCTGAGC AGGGATTAAG AGCTTGGGCT CTCATATGGT                 | <CREB <ER            |
| -1402    | GTTTCTGGGC TCAACTGCCA GCTCCGTCAC TTAAGTGGTG CTGTGACCAT                 |                      |
| -1352    | GGGCAAGTTA TTCCATCTCT CCATATCTCT TTCCTCACTT TTAATATGGA                 |                      |

Figure 1, page 3

C4  
Kpn I

```

-1302 ATAATGGGGT ACCCACCTCC CAGGGTCACA GAGAGGCTTA CAGAAAACGA
      NF-1>
-1252 TTCTTGTGAA TTGGCTTGCA GTAATAATTC AATACCTGCC AGCTATTCTT
      <PPAR-α <Oct-1
-1202 ATTCCACATC CAAGCCCTTT CGCCTGCTGC TGGGTGAAAA CACATGTCAG
      CREB/ATF> <STAT <C/EBP-β
-1152 TGTTTCCTGA CGGTTCCTCCAC AAAGAAGATT CCAAAATTAC AACCTGCCAG
-1102 TCTGAAGAAT CTCCAAAACA TCCCGCACGC ATCCTGGAGG CGCGGGCTTG
      <SP-1
      NF-kB> <NF-kB
-1052 GGGATGGGAC TGCCCGCCCCG GGTCTGAAC AGGATGCGTG CGCGCAGGCA
      Ets-1>
-1002 CACACACACC AGCCAGCCTG TGTGTGCGGC CGGAGTCCGG TCGGTCCCCG
      <Myc/Max
      <Whn SP-1>
-952 GGTGAGCAGC GCGTGGCTGG TGGGCGGGGC AGAGCCATTG TTCGCAGGCG
      C5
      Sma, I
      ~~~~~ NF-kB> <NF-kB<Whn
-902 TACCGAGCCC CCCGCGCTCG CCCGGGAGGG AGGCGGGGCT TCCCGCGTCC
      Myc/Max>
      Whn>
-852 CCAAGCTCCA GATCCTGGGG TGGCTGCCAC GTCTCCCTGC CACGCGCCTG
      <AP-2 c8
-802 GGGGGACGGG AAGACGGGAC GGAGATGTTA GTGGTGGGCG CCCCCGAGG
      <RFX-1 RFX-1> NF-kB>
-752 GTTCACTACT GTTTCCTGAG AAACCTCCCC AGTGCCCACC CACCCGTTCT
      AP-2>
-702 CCGTGTGCCC GAGGGCCGGT CCTGGGCTAG GCTCCGCGCC CCAGCCCCAA
      Whn> c9
-652 ACCGGGTCCC CAGCCCCTTC CAGAGAGAAA GCTCCCGACG CGGGATGCCG
      AP-2> ISRE>
-602 GGCAGAGGCC CAGCGGCGGG TGGAAGAGAA GCTGAGAAGG AGAAACAGAG
      SP1> RFX1> SREBP>
-552 GGGAGGGGGA GCGAGGAGCT GCGGCAGAG GGAACAGCAG ATTGCGCCGA
      <NF-1
      c6 NF-Y>
      <NF-1 C10 Eae I CREB>
      NF-Y> RFX-1> ~~~~~ AP-1>
-502 GCCAATGGCA ACGGCAGGAC GAGGTGGCAC CAAATTCCT TCGGCCAATG
      <C/EBP-β <Oct-1 GC box>
-452 ACGAGCCGGA GTTTACAGAA GCCTCATTAG CATTTCCCCA GAGGCAGGGG
      EBV>
-402 CAGGGGCAGA GGCCGGGTGG TGTGGTGTCT GTGTCGGCAG CATCCCCGGC

```

[illegible]

Sub  
A6

[illegible]

Sub

| Year | 1970 | 1971 | 1972 | 1973 | 1974 | 1975 | 1976 | 1977 | 1978 | 1979 | 1980 | 1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 | 2036 | 2037 | 2038 | 2039 | 2040 | 2041 | 2042 | 2043 | 2044 | 2045 | 2046 | 2047 | 2048 | 2049 | 2050 | 2051 | 2052 | 2053 | 2054 | 2055 | 2056 | 2057 | 2058 | 2059 | 2060 | 2061 | 2062 | 2063 | 2064 | 2065 | 2066 | 2067 | 2068 | 2069 | 2070 | 2071 | 2072 | 2073 | 2074 | 2075 | 2076 | 2077 | 2078 | 2079 | 2080 | 2081 | 2082 | 2083 | 2084 | 2085 | 2086 | 2087 | 2088 | 2089 | 2090 | 2091 | 2092 | 2093 | 2094 | 2095 | 2096 | 2097 | 2098 | 2099 | 2100 |
|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| 1970 | 1971 | 1972 | 1973 | 1974 | 1975 | 1976 | 1977 | 1978 | 1979 | 1980 | 1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 | 2036 | 2037 | 2038 | 2039 | 2040 | 2041 | 2042 | 2043 | 2044 | 2045 | 2046 | 2047 | 2048 | 2049 | 2050 | 2051 | 2052 | 2053 | 2054 | 2055 | 2056 | 2057 | 2058 | 2059 | 2060 | 2061 | 2062 | 2063 | 2064 | 2065 | 2066 | 2067 | 2068 | 2069 | 2070 | 2071 | 2072 | 2073 | 2074 | 2075 | 2076 | 2077 | 2078 | 2079 | 2080 | 2081 | 2082 | 2083 | 2084 | 2085 | 2086 | 2087 | 2088 | 2089 | 2090 | 2091 | 2092 | 2093 | 2094 | 2095 | 2096 | 2097 | 2098 | 2099 | 2100 |      |

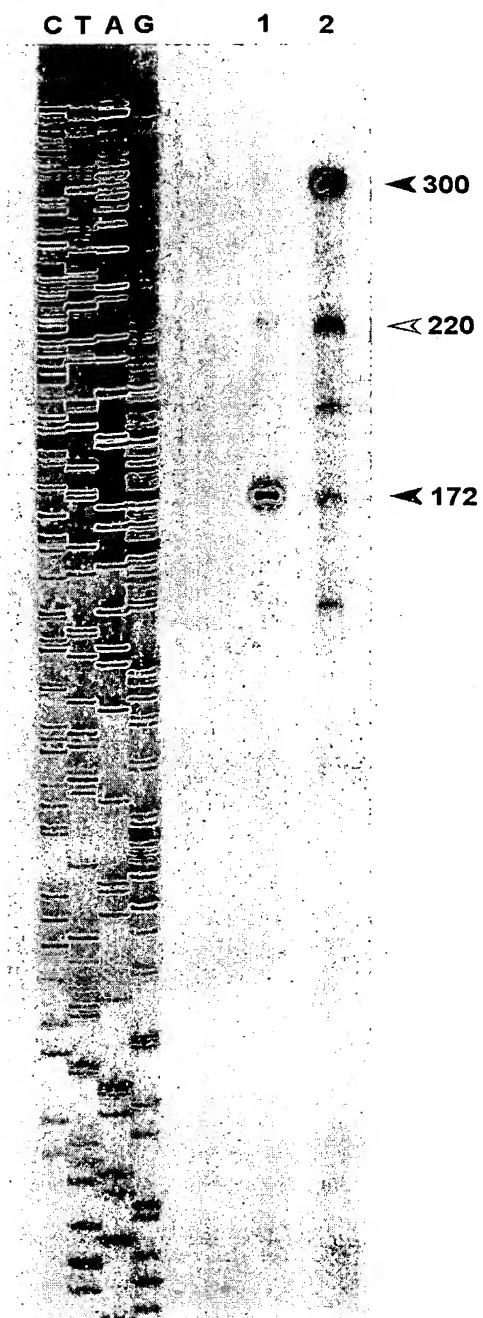
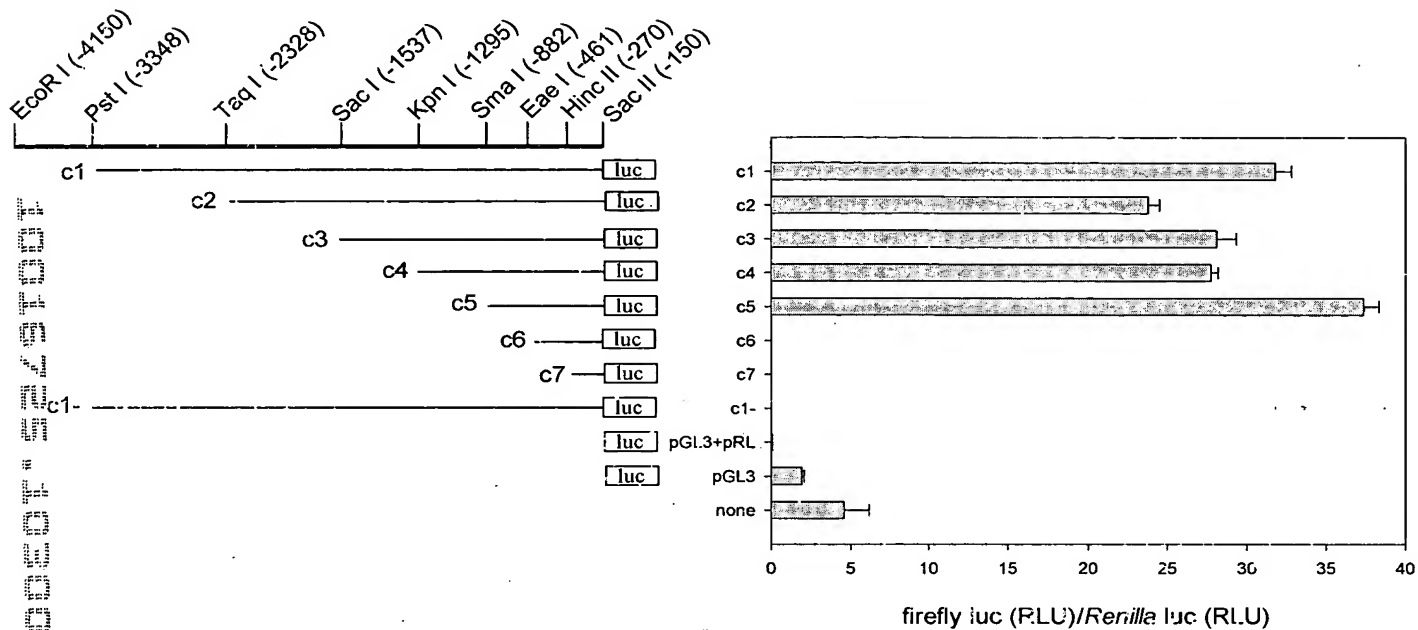


Figure 3

Figure 4



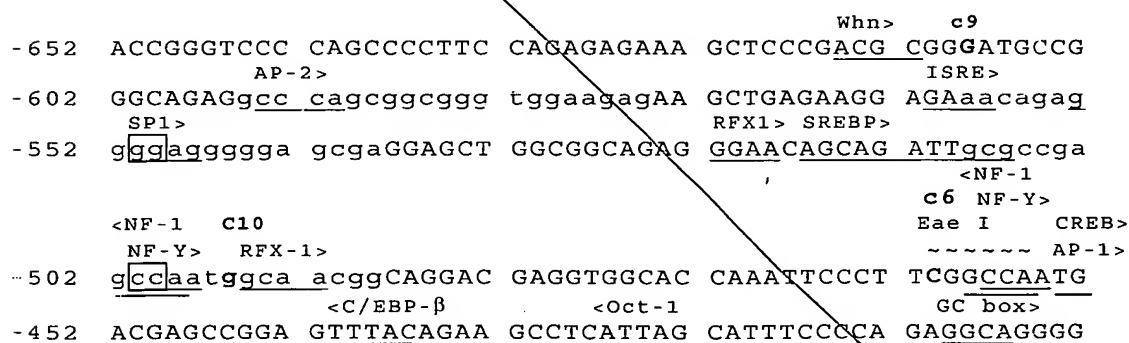
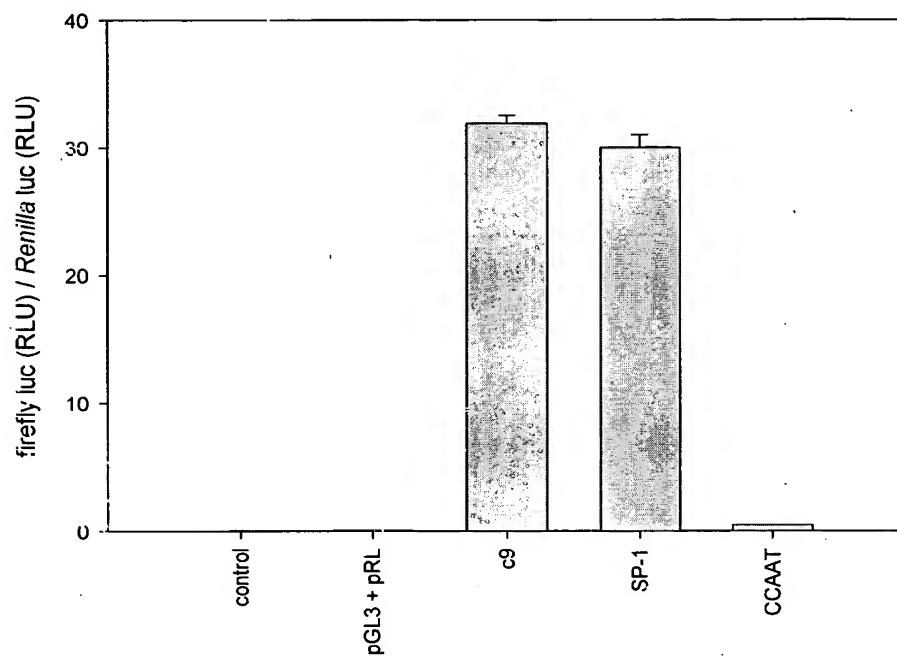


Figure 5



Figure 6



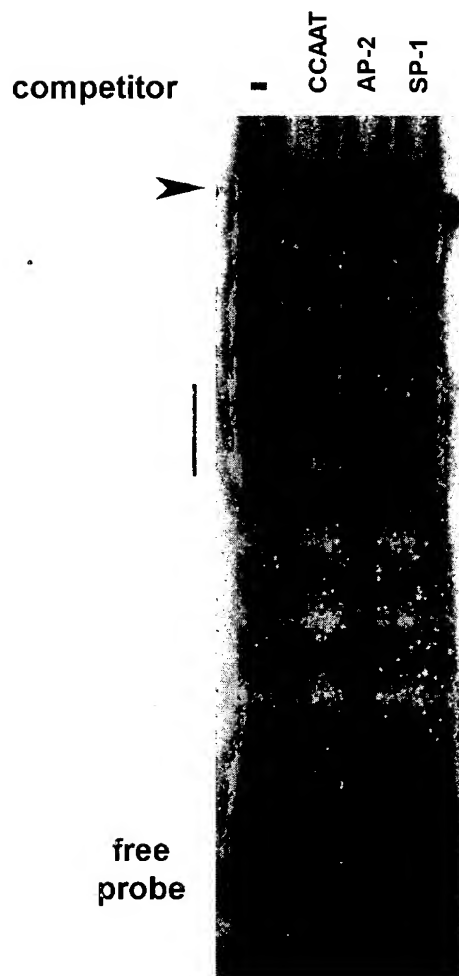


Figure 7

[illegible]

Sub  
A6

[illegible]

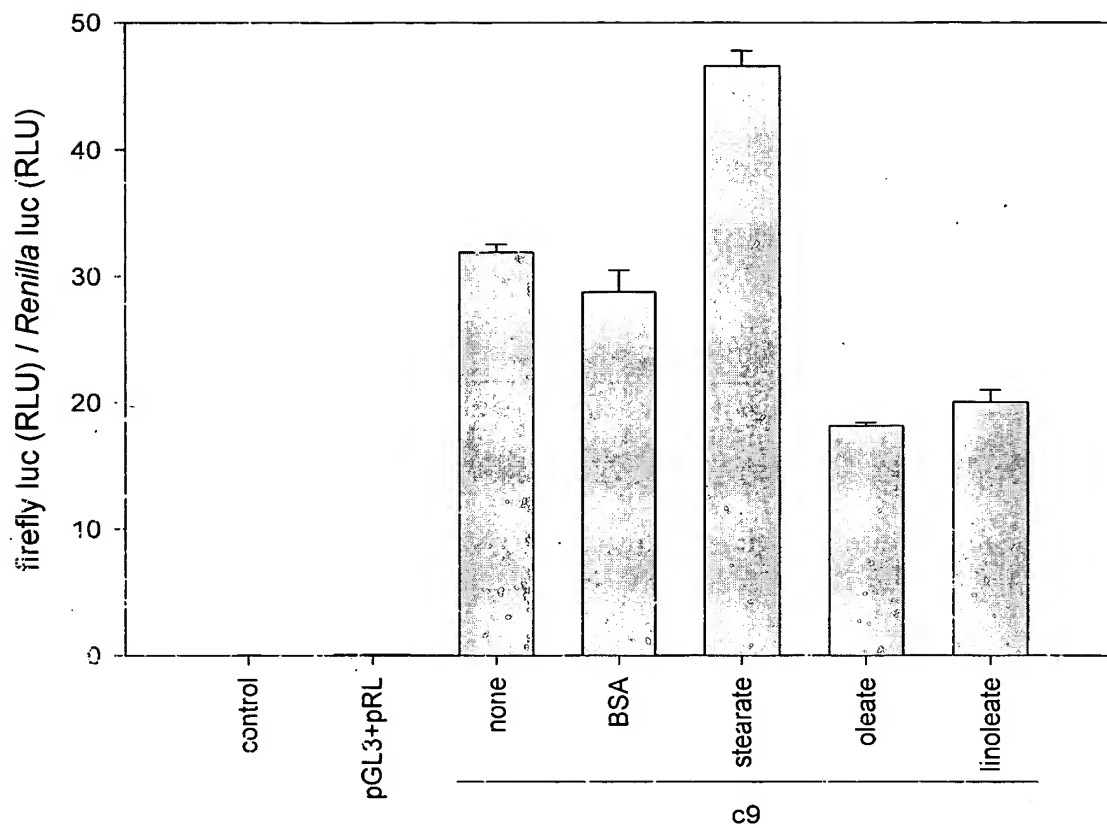


Figure 9